RESEARCH ARTICLE

CLINICAL PROFILE OF DENGUE FEVER IN TERTIARY HOSPITAL, NELLORE

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ABSTRACT

Objective: Dengue viral infections are among the most important mosquito borne diseases of the Indian subcontinent and have become a major global public health concern. The objective was to study the clinical, biochemical profile and complications of dengue fever.

Methodology: This prospective study was conducted in the Department of General Medicine at Narayana Medical College & Hospital, Nellore during the recent epidemic of Dengue fever in Andhra Pradesh from September – December 2015. All the patients who were suspicious cases of Dengue fever and who fulfilled were included in the study.

Results: Of the 366patients admitted with probable dengue fever, 170 patients were serologically confirmed as dengue fever. Of these 170 cases, most of the cases were male (54.7%), and the most common age group was 21-30 years. The most common presentation was fever in 170 (100%), followed by vomitings (44.7%), myalgia (30.5%), abdominal pain (28.8%) and headache (25.8%).Most common hemorrhagic manifestation was malena (9.4%). On examination hepatomegaly in 45 patients (26.5%) and splenomegaly (15.3%) were observed. NS1 Ag positive in 141 patients(82.9%), IgM positive in 22 patients (12.9%) and IgG positive in 7 patients (4.1%) by Immunochromatographic test (J. Mitra, India). Leucopenia was seen in majority (71.7%) of the patients. Elevated hematocrit was seen in 48 patients (28.2%), AST in13 patients (7.6%), ALT in 22 patients (12.9%) and creatinine in 33 patients (19.4%). Thrombocytopenia was the single most common hematological abnormality noted in 149patients (87.6%). Radiologically GB wall distention (56.4%), hepatomegaly (26.5%) and Ascites (18.2%)was observed. Dengue Fever was present in 133(66.7%), DHF in 42 (24.7%) and DSS in 15 (8.6%).Out of 170 patients most of them had, acute kidney injury (19.4%), hepatitis (16.5%), ARDS(4.5%) and multi organ dysfunction in 7 patients (4.1%), pancreatitis (2.35%) and bell's palsy in two patients

Conclusion: Fever, vomiting and malaise are the common manifestations. They should prompt a clinician on the possibility of dengue infection. Awareness and timely recognition of the atypical & hemorrhagic manifestations are very important for proper management especially in Dengue fever.

INTRODUCTION

Dengue is a mosquito borne viral infection caused by dengue viruses (DENVs). It is the most common and the most rapidly growing mosquitoborne viral infection worldwide (Chakravarti et al., 2012). Dengue incidence has increased 30fold. DENV are ubiquitous throughout thetropics, with local spatial variations in risk influenced by temperature, rainfall and the degree of urbanization (WHO, 2009). Dengue was first reported in 1780, when Benjamin Rush described this condition as

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"break-bone fever." Dengue is transmitted by mosquitoes of the genus Aedes, principally Aedesaegypti (Bhatt et al., 2013). All the four serotypes have been isolated in India (i.e) Dengue 1,2,3&4 (Murray et al., 2013). In 2015 a total of 97740 cases were confirmed and a total of 200 deaths occurred as per NVDCP statistics (http://nvbdcp.gov.in/dencd.html).

In 2009, the World Health Organization (WHO) updated and categorized the new dengue definitions into dengue without warning signs, dengue with warning signs, and severe dengue (Table 1).

Table 1. The 2009 WHO classification for dengue severity

Criteria for dengue± warning signs		Criteria for severe dengue
Probable dengue Live in /travel to dengue Endemic area. fever and 2 Signs of following criteria	Warning Signs	Severe Plasma Leakage
1. Nausea, vomiting	1. Abdominal pain or Tenderness	1. Shock (DSS)
2. Rash	2. Clinical fluid accumulation	2. Fluid accumulation with respiratory distress
3. Aches and pains	3. Mucosal bleed	3.Severe Bleeding as evaluated by clinican
4. Tourniquet test positive	4. Lethargy, restlessness	Severe organ involvement
5. Leukopenia	5. Liver enlargement>2cm	4. Liver : AST or ALT>=1000
6. Any warning signs	6. Laboratory: increase HCT concurrent with rapid Decrease in platet count	5. CNS : Impaired consciousness
Laboratory-confirmed dengue (important when no sign of plasma leakage)	*(requiring strict observation and medical intervention)	6. Heart and other organs

According to the US Centers for Disease Control and Prevention (CDC) and the WHO dengue guidelines (WHO 1997), the clinical features of DF and DHF are sudden onset of fever, severe headache, myalgias and arthralgias, leucopenia, thrombocytopenia, and hemorrhagic manifestations. It occasionally produces shock and haemorrhage, leading to death. Classic DF symptoms include fever, headache, retro-orbital pain, myalgias and arthralgias nausea, vomiting, and often a rash. Some DF patients develop the more serious form of the disease DHF with symptoms that include a decline in fever and presentation of hemorrhagic manifestations, such as microscopic hematuria, bleeding gums, epistaxis, hematemesis, malena, and ecchymosis. DHF patients develop thrombocytopenia and hemoconcentration; the latter is due to an increase in the concentration of blood cells resulting from the leakage of plasma from the bloodstream. These patients may progress into DSS, which can lead to profound shock and death if not treated. Advance clinical symptoms of DSS include severe abdominal pain, protracted vomiting, and a notable change in temperature from fever to hypothermia (http://www.cdc.gov/ncidod/dvbid/dengue/dengue-hcp.htm).

The present study was conducted to evaluate the clinical profile of Dengue fever in age between 16 – 60years during the recent epidemic in Nellore during period September – December 2015.

MATERIALS AND METHODS

Study Design: We included all suspected dengue patients of 16 years or older admitted to medical wards and who appeared to have acute febrile illness with myalgia, arthralgia, headache, malaise, abdominal pain, nausea and vomiting, bleeding, hypotension or thrombocytopenia. A detailed history as well as a general and systemic clinical examination (including the tourniquet test) was recorded.

Study Area: This case series was conducted at the Department of General Medicine in Narayana Medical College, Nellore, from the patients admitted with Dengue fever from September – December 2015.

Inclusion Criteria: All patients above 16 years of age

Exclusion Criteria: The patients with concomitant malaria, typhoid, leptospirosis, patients who were suffering from fever and thrombocytopenia due to any chronic illness like aplastic anemia, acute leukemia, hypersplenism, chronic liver disease, Pregnant women and age less than 16 years were excluded from the study.

Laboratory Investigations: Hemoglobin, total and differential leucocyte counts, platelet count with coagulation profile (PT, aPTT), hematocrit, liver function tests, blood urea and serum creatinine, chest radiograph and ultrasound scan of abdomen. Platelet counts were monitored periodically. Dengue serological confirmatory test was performed using Immunochromato graphic test (J. Mitra, India) for NS1, IgM and IgG.

RESULTS

A total of 366 patients who reported between September to December 2015 were studied and analysed. Majority of these cases reported to our hospital coinciding with rainy season, showing the breeding of mosquitoes during the said period. Of the 366 patients admitted with probable dengue fever, 170 patients were serologically confirmed as dengue fever. Of these 170 cases, most of the cases were male (54.7%), and most of the cases fall in the age group of 21 – 30 years .The most common presentation was fever in 170 (100%), followed by vomiting in 76 (44.7%), malaise in 52 (30.5%), abdominal pain in 49 (28.8%), hepatomegaly 45 (26.5%), splenomegaly 26 (15.3%) and headache 44 (25.8%) cases. Malena was the most common hemorrhagic presentation (9.4%),while bleeding from skin was documented in 13 patients (7.64%), hematuria in 6(3.5%), hemetemesis and bleeding gums each in two patients. Out of 170 cases NS1 Ag positive in 141 patients (82.9%), IgM positive in 22 patients (12.9%) and IgG positive in 7 patients (4.1%) by Immunochromatographic test (J. Mitra, India)for NS1, IgM and IgG. Majority of these cases had Leucopenia (71.7%) followed by normal count in 16.4% and leucocytosis seen in 20 patients (11.7%). Elevated Serum creatinine (19.4%), transaminases like AST (7.6%), ALT(12.9%)) and BILURUBIN (16.5%) was seen in this study. In the present study, 28.2% patients had elevated hematocrit (>40) out of 170 patients. In the present study we encountered 87.6% had thrombocytopenia, more number of patients(34.7%) were in severe thrombocytopenia (<50000/cumm) followed by moderate(30%) and mild (22.9%) which was depicted in Table 5. Radiologically we found edematous gallbladder (GB) wall thickening, was the most common finding (56%) followed by hepatomegaly (26.5%), ascites (18.2%), splenomegaly(15.3%) and pleural effusion in 14 patients.
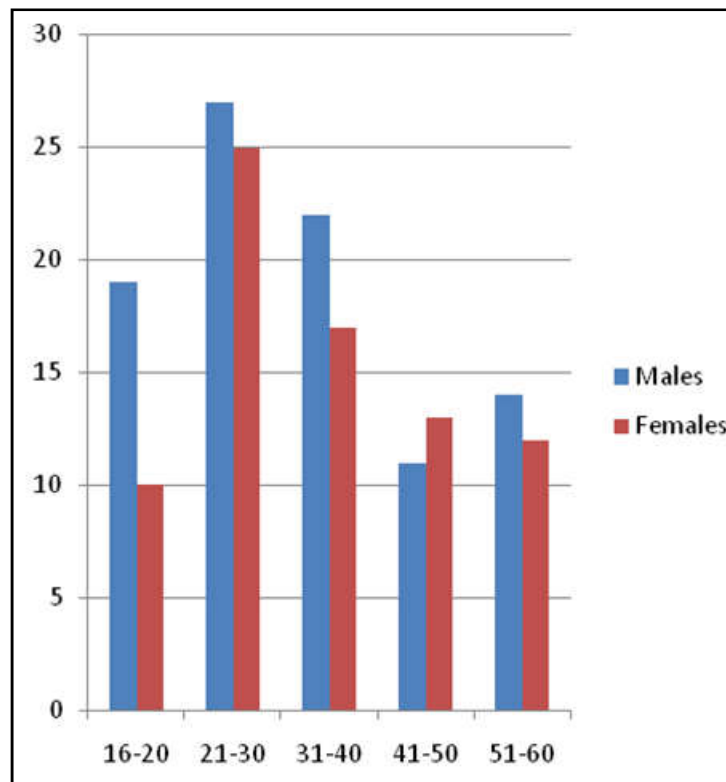
Figure 1. Age & Sex Characteristics

Table 2. Clinical Features

Clinical Feature:	No. of Patients (%)
Fever	170 (100)
Vomiting	76 (44.7)
Myalgia	52 (30.5)
Abdominal pain	49 (28.8)
Headache	44 (25.8)
Cough	34 (20.0)
Chills	16 (9.41)
Diarrhea	14 (8.23)
Malaise	12 (7.05)
Nausea	11 (6.47)
Hepatomegaly	45 (26.5)
Splenomegaly	26 (15.3)

Table 3. Hemoglobin, Renal Function Test (RFT), Liver Function Test (LFT)

	Normal (%)	Abnormal (%)	Mean	Standard Deviation
1. Hemoglobin	118(69.41)	52(30.5)	-	-
2. S.Creatinine	137(80.58)	33(19.41)	1.53	1.15
3. S.Bilurubin	142(83.5)	28(16.5)	1.57	1.07
4. AST	157(92.4)	13(7.6)	51.87	82.65
5. ALT	148(87.05)	22(12.94)	55.32	82.97

Table 4. Packed Cell Volume (PCV)

<40%	122(71.76)
>40%	48(28.23)

Table 5. Platelet Count

Platelet Count	No. of Patients(%)
1. >1,50,000	21(12.35)
2. 1,00,000 - 1,50,000	39(22.9)
3. 50,000 - 1,00,000	51(30)
4. <50,000	59(34.7)

Figure 2. Bleeding Manifestations

Figure 3. Serological Confirmation

Figure 4. Total Lecukocyte Count (TLC)
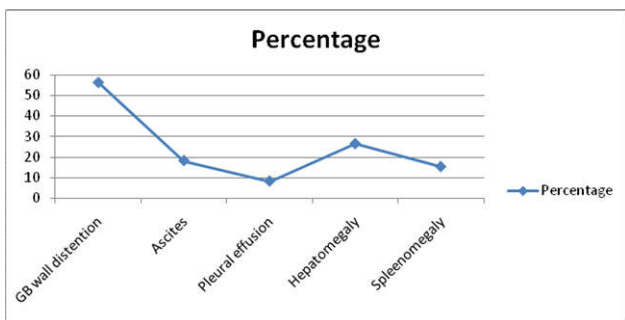
Figure 5. Radiological Investigation

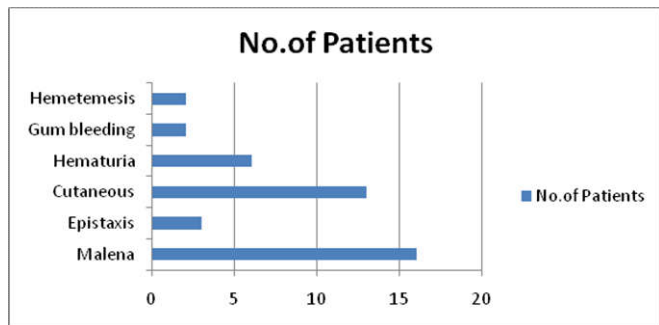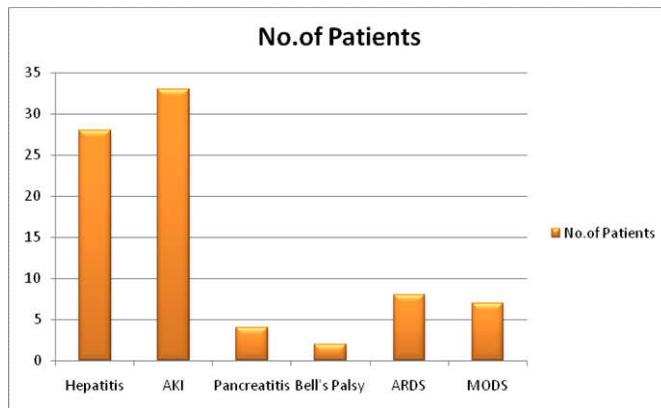**Figure 6. Groups**

Figure 7. Complications

Of 170 cases, Dengue Fever was present in 133(66.7%), DHF in 42 (24.7%) and DSS in 15 (8.6%). In our study, more number of dengue cases had Acute kidney injury (19.4%) followed by hepatic dysfunction (16.5%), ARDS (4.5%), Multi organ failure (4.1%), Pancreatitis (2.3%) and Bell's palsy in two patients. Mortality was in seven patients and mean duration of hospital stay was 4.8 days in the present study.
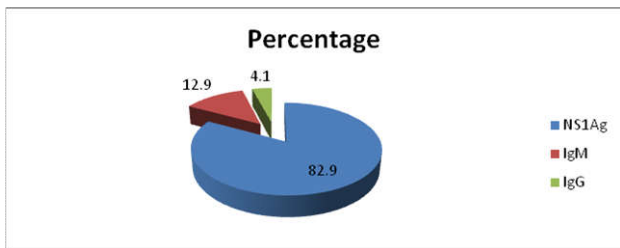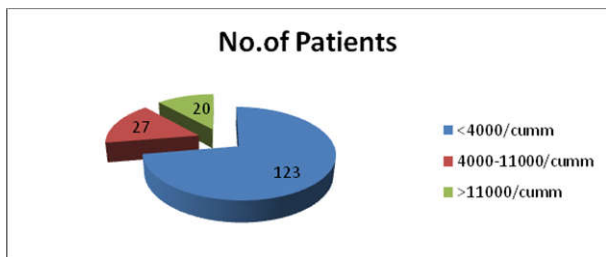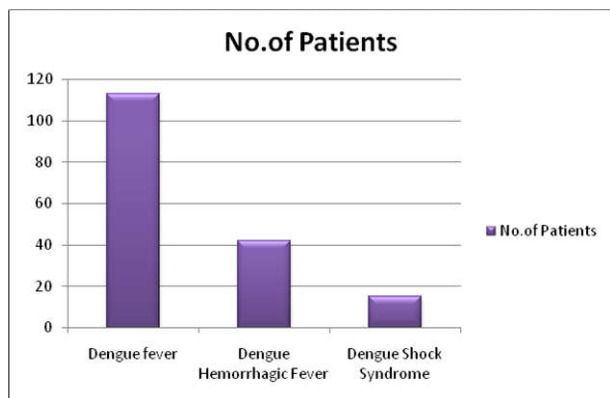
DISCUSSION

Of 366 cases included in this study who were confirmed as a dengue in 170(46%) patients, 93 (54.7%) were males and 77(45.3%) were females. fifty-two patients (30%) were in the age group of 21-30 years. According to Karoli *et al*, enrolled 356 patients of suspected dengue fever of whom 138 (39%) were serologically confirmed to have dengue infection (Karoli *et al*., 2012). Eighty (58%) patients were males and 58 (42%) were females. Kumar *et al*, in their study in North Karnataka reported a higher number of cases of DF in 14-30 years age group (Kumar *et al*., 2015). Kashinkunti *et al*. 54% were males and 46% were females. Maximum number of cases 61% was in the age group of 15–40 years (Mohan *et al*., 2013). In Saqib *et al*. conducted in Lahore, 70% were males and 30% of the cases were between 20years and 29 years (Saqib *et al*., 2014). Thus, the disease affects the young people, mostly males, which may be because they are more often outdoors and working. Fever was the most common presentation (100%), which was similar with studies from India and South East Asia, followed by vomiting (44%), myalgia (30%), abdominal pain (28%), headache (25%) (Srikiatkhachorn *et al*., 2010; Mohan *et al*., 2013; Rachel *et al*., 2005; Munde and Shetkar, 2013). Only a small number of subjects experienced chills and rigor, but Anuradha *et al*. showed that fever was of high grade with chills and rigors (Anuradha *et al*., 1996). Munde *et al* in their series of patients have shown myalgia in 50% and headache in 25% of all patients (Munde and Shetkar, 2013). According to Rathore *et al*. fever was the main complaint in all the cases of dengue, followed by vomiting, headache and abdominal pain was reported in 43.48%, 40.55%, and 30.82% of cases, respectively in Indian series which was closely related to the present study (Rathore *et al*., 2015). Out of 170 patients,42(24.7%) patients had bleeding manifestations, among them most common was malena (9.4%); followed by cutaneousin the form of petechiae, purpura, ecchymosis (7.64%), hematuria (3.52%), gum bleeding (1.17%), and hematemesis in 2 patients. In Rathore

et al petechiae, gum bleeding and other bleeding manifestations were reported in 20.55% dengue cases. Kashinkunti *et al*., Kumar *et al*., also reported 21% and 19.5% bleeding manifestation, respectively, in their study. Mandal *et al*., in their study reported bleeding gums and malena among 13.51% patients (Mandal *et al*., 2013). In Rajesh *et al*. while bleeding in the form of petechiae, ecchymosis and epistaxis was documented in 5.43% of cases which were almost similar in the present study (Rajesh Deshwal *et al*., 2015). Among confirmed of dengue cases,141(82.9%)were positive for NS1Ag, 22(12.9%) were for IgM and IgGwas seen in only seven (4.1%) by using a commercially available Immuno-chromatographic test for NS1 antigen, IgM and IgG antibodies (J. Mitra, India). According to Chakraverti *et al*. who compared simultaneously the performance of two commercially available ELISA and ICT based test for the early diagnosis of dengue was no "statistically significant" difference found between ELISA and ICT (Chakraverti *et al*., 2012).

As Leucopenia or normal count was common finding in Dengue fever 71.7% and16.4%were also seen respectively in the present study. According to Karoli *et al* and Ahmed *et al*; in their study86% and 68.9% patients had leucopenia respectively which were similar to the present study (Maimoona M. Ahmed, 2010). Leucocytosis (11.7%) which was observed, due to may be complications of dengue fever. Elevated Serum creatinine (19.4%), transaminases like AST(7.6%), ALT(12.9%) and bilirubin(16.5%) was seen in this study, shown in Table 3.In Karoli *et al*, out of 138 patients 127(92%) had raised transaminases, and study done by Manish *et al*, noticed 50%of their patients had elevated transaminases and deranged RFT by 25% (Manish Ramesh Patil *et al*., 2016). In the present study we noticed less number of patients had raised transaminases and deranged RFT. This is may be due to early presented to the hospital, geographical variation, immune status, age and sex variation. In the present study, 48 (28.2%) patients had elevated hematocrit(>40) out of 170 patients, this was also seen in study done by Karoli *et al*, in which out of 138 patients 42 (30%) had signs of plasma leakage. As depicted in Table5, 87.6% patients had thrombocytopenia, which were similar with others by Karoli *et al*, Hassan *et al* and Mumtaz *et al* (ie. 89%, 85% and83% respectively) more number of patients(34.7%) were in severe thrombocytopenia (<50000/cumm) followed by moderate (30%) and mild (22.9%) with lowest platelet count 4000/cumm in the present study. These platelet counts kept on falling further during hospitalization or observation. Bleeding manifestations were seen in severe thrombocytopenia, but not correlated with their platelet count, this was also similar with study done by Chairulfatah *et al*. (2003). According to Jain *et al*, 80% patients had platelet count below 100,000/cumm and 47 patients (41.2%) had platelet count below 50,000/cumm, closely related to this study (Jain *et al*., 2015). Bone marrow suppression, immune mediated clearance, spontaneous aggregation of platelets to virus infected endothelium; all may contribute to thrombocytopenia. Radiologically we found edematous gallbladder (GB) wall thickening, was the most common finding (56%) followed by hepatomegaly (26.5%), ascites (18.2%), splenomegaly (15.3%) and pleural effusion in 14 patients. These patients had shown multiple combinations of above features with varying degree of severity. These features

were also seen in other studies by Rajesh *et al*, Santhosh *et al*. (2014) and Tewari *et al*. (2013). According to the current WHO (2009) classifications, all patients were classified as having dengue with warning signs or severe dengue. In the present study, Dengue fever was seen in 66.7% of the study population. The incidence of DHF and DSS was 24.7% and 8.6% respectively. In a study done by Neerja *et al*. the prevalence of DF, DHF, DSS was 85%, 5%, 10% respectively (Neeraja *et al*., 2006). In a study done by Pancharoen *et al* there was high incidence of DHF i.e., 60.4% (Panchareon and Thisyakora, 2001). The results of the present study corresponds to a study by Fazal *et al*, Dengue fever was seen in 70%, DHF and DSS was 23%and 7%respectively (Farhan fazal and Sangram Birdar, 2015). From these observations, we can conclude that the incidence of each clinical spectrum varies with geographical area. In our study, more number of dengue cases had Acute kidney injury (19.4%) and hepatic dysfunction(16.5%) as a complications which were also similar in other studies by Srinivasulu *et al*. (2016). And Kashinkunti *et al*. But we had two rare complications of dengue fever were Bell's palsy in two patients and Pancreatitis in four patients. Dengue fever can give rise to various neurological manifestations like GB syndrome, encephalopathy, ADEM, Lumbosacral plexopathy, polyradiculopathy etc as evidenced by various studies. Neurological involvement in dengue may occur because of neurotropism of the virus, immunologic mechanism, cerebral anoxia, intracranial haemorrhage, hyponatremia, cerebral oedema, fulminant hepatic failure with portosystemic encephalopathy, renal failure or release of toxic products. Mandal *et al*, found 11.11% in the form of encephalopathy (2.7%), GB syndrome (2.7%) and facial nerve palsy (1.35%) and lateral rectus palsy (4.05%). MRI of Brain had taken in both cases which showed normal study, they were spontaneously recoverd from the bell's palsy in the present study. Among four patients of Pancreatits, we were ruled out all the causes of pancreatits, Three patients had highly elevated lipase and amylase levels, were confirmed by CECT abdomen. More interestingly one patient had with normal enzymes, on clinical suspicion by Gastroenterologist took CECT Abdomen showed bulky pancreas with peripancreatic fluid and calcifications. This case was reported as a rare combination in dengue fever. All patients were received supportive therapy in the form of Antipyretics, Antibiotics those who were in complications, platelet and blood transfusions who had bleeding diathesis, Intravenous fluids and mechanical ventilation support in cases of ARDS and Multi organ failure. We noticed Mortality in seven (4.1%) patients, remaining were discharged satisfactorily. Mean duration of hospital stay was 4.8 days.

Conclusion

Fever, vomiting, headache, hepatosplenomgaly and malaise are the common manifestations .They should prompt a clinician on the possibility of dengue infection. Awareness and timely recognition of the atypical & hemorrhagic manifestations are very important for proper management especially in Dengue fever. Early diagnosis, careful monitoring and proper fluid management goes a long way in reducing the mortality due to dengue hemorrhagic fever and shock syndrome.

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